

=> d his

(FILE 'HOME' ENTERED AT 17:00:46 ON 07 NOV 2005)

L1 FILE 'REGISTRY' ENTERED AT 17:00:53 ON 07 NOV 2005
1 S NATEGLINIDE/CN

L2 FILE 'REGISTRY' ENTERED AT 17:01:19 ON 07 NOV 2005
STR 105816-04-4
L3 35 S L2 FAM FUL
L4 1 S C19 H27 N O3 . X C2 H4 CL2/MF AND L3

L5 FILE 'CAPLUS' ENTERED AT 17:03:13 ON 07 NOV 2005
1 S L4
L6 418 S L3

L7 FILE 'REGISTRY' ENTERED AT 17:04:51 ON 07 NOV 2005
1 S C19 H27 N O3 . X C3 H8 O/MF AND L3

L8 FILE 'CAPLUS' ENTERED AT 17:05:01 ON 07 NOV 2005
1 S L7
L9 3 S L6 AND SOLVAT?

=> s 16 and crystal?
1696384 CRYSTAL?
L10 28 L6 AND CRYSTAL?

=> s 110 not (18 or 19)
L11 25 L10 NOT (L8 OR L9)

=> d bib hit 25 hitstr

L11 ANSWER 25 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
AN 1993:261002 CAPLUS
DN 118:261002
TI Stable **crystals** of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine
IN Sumikawa, Michito; Koguchi, Yoshihito; Ohgane, Takao; Irie, Yasuo; Takahashi, Satoji
PA Ajinomoto Co., Inc., Japan
SO Eur. Pat. Appl., 14 pp..
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 526171	A2	19930203	EP 1992-306895	19920729
	EP 526171	A3	19930505		
	EP 526171	B1	19970305		
	R: AT, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
	JP 05208943	A2	19930820	JP 1992-202686	19920729
	JP 2508949	B2	19960619		
	AT 149483	E	19970315	AT 1992-306895	19920729
	ES 2100291	T3	19970616	ES 1992-306895	19920729
	CA 2114678	AA	19950802	CA 1994-2114678	19940201
	CA 2114678	C	19990427		
PRAI	JP 1991-189696	A	19910730		
	JP 1991-199453	A	19910808		
TI	Stable crystals of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine				
AB	Stable H-type crystals of N-(trans-4-				

isopropylcyclohexylcarbonyl)-D-phenylalanine (I) are obtained by treating I with a solvent, at >10°. A solution of 5 g I in 20 mL acetone was added to a stirred mixture of 40 mL acetone and 60 mL water, at 25° to precipitate H-type **crystals**. The **crystals** have different m.p., IR spectrum and x-ray diffraction patterns from known forms of I and are not converted to other forms when ground.

ST phenylalanine deriv drug stable **crystal**

IT 105816-04-4P

RL: PREP (Preparation)

(**crystals**, stable, preparation of)

IT 105816-04-4P

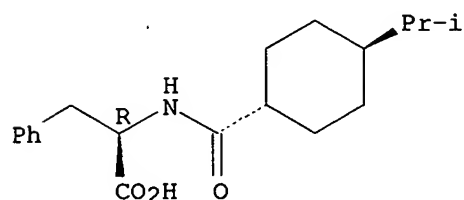
RL: PREP (Preparation)

(**crystals**, stable, preparation of)

RN 105816-04-4 CAPLUS

CN D-Phenylalanine, N-[[trans-4-(1-methylethyl)cyclohexyl]carbonyl]-. (9CI)
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



=> d bib hit 1-24

L11 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:467801 CAPLUS

DN 143:7982

TI Process for the preparation of the **crystalline** B-form nateglinide from D-phenylalanine methyl ester and trans-4-isopropylcyclohexanecarboxylic acid

IN Vigano', Enrico; Pizzati, Enrica; Lanfranconi, Simona; Molteni, Renato; Landonio, Ernesto

PA A.M.S.A. Anonima Materie Sintetiche e Affini S.p.A., Italy

SO Eur. Pat. Appl., 32 pp.

CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1535900	A1	20050601	EP 2003-27114	20031126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI EP 2003-27114		20031126		

OS CASREACT 143:7982

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Process for the preparation of the **crystalline** B-form nateglinide from D-phenylalanine methyl ester and trans-4-isopropylcyclohexanecarboxylic acid

ST nateglinide prepn polymorphic **crystal** B form

IT Polymorphism (**crystal**)

(process for the preparation of the crystalline B-form nateglinide from D-phenylalanine Me ester)

IT 105816-04-4P, Nateglinide
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(process for the preparation of the crystalline B-form nateglinide from
D-phenylalanine Me ester)

L11 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:216663 CAPLUS
DN 142:266828
TI Preparation of pharmaceutical compositions of nateglinide
IN Singh, Romi Barat; Shilpa, Anu; Nagaprasad, Vishnubhotla; Sethi, Sanjeev
Kumar
PA Ranbaxy Laboratories Limited, India
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005020979	A1	20050310	WO 2004-IB51678	20040902
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI IN 2003-DE1100 A 20030903
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Antidiabetic agents
Binders
Diabetes mellitus
Dyes
Fillers
Flavoring materials
Granulation
Lubricants
Milling (size reduction)
Particle size distribution
Polymorphism (**crystal**)
Surfactants
(preparation of pharmaceutical compns. of nateglinide)
IT 657-24-9, Metformin 1327-43-1, Magnesium aluminum silicate 1343-88-0, Magnesium Silicate 2295-31-0D, 2,4-Thiazolidinedione, derivs. 9004-32-4 9004-34-6D, Cellulose, derivs. 14987-04-3, Magnesium trisilicate 74811-65-7, Croscarmellose sodium 105816-04-4, Nateglinide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of pharmaceutical compns. of nateglinide)

L11 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:59980 CAPLUS
DN 142:141289
TI **Crystalline** form of nateglinide
IN Frenkel, Gustavo; Gome, Boaz; Wize, Shlomit
PA Israel
SO U.S. Pat. Appl. Publ., 91 pp., Cont.-in-part of U.S. Ser. No. 622,905.

CODEN: USXXCO

DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2005014836	A1	20050120	US 2003-746697	20031224
	US 2004181089	A1	20040916	US 2003-622905	20030718
	CA 2513753	AA	20040812	CA 2004-2513753	20040113
	WO 2004067496	A1	20040812	WO 2004-US839	20040113
	WO 2004067496	C2	20041209		
	W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
	EP 1511717	A1	20050309	EP 2004-701826	20040113
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	US 2003-442109P	P	20030123		
	US 2003-449791P	P	20030224		
	US 2003-479016P	P	20030616		
	US 2003-622905	A2	20030718		
	US 2002-396904P	P	20020718		
	US 2002-413622P	P	20020925		
	US 2002-414199P	P	20020926		
	US 2002-423750P	P	20021105		
	US 2002-432093P	P	20021210		
	US 2002-432962P	P	20021212		
	WO 2003-US22375	A	20030718		
	US 2003-693166	A	20031023		
	US 2003-746697	A	20031224		
	WO 2004-US839	W	20040113		

TI **Crystalline** form of nateglinide

AB Crystalline forms of nateglinide and processes for their preparation, as well as

pharmaceutical formulations containing them and methods of administration are provided. A process for preparing crystalline form of nateglinide comprises

the

steps of (a) preparing a solution of nateglinide in Et acetate, (b) seeding the solution with nateglinide **crystals**, and (c) recovering the crystalline form as a precipitate. The nateglinide obtained is more than about 99% pure.

For

example, nateglinide (5 g) was dissolved in acetonitrile, acetone, or Et acetate at about 55° in over about 15 min until a clear solution was obtained. The solvent was removed to dryness by evaporation at about 55°/20 to 30 mmHg to give dry nateglinide crystalline Form B. Also, nateglinide Form Z was prepared by treating 7.73 g of D-phenylalanine (PheOH) with 185 mL (3.5 equiv) of 3.5% NaOH at room temperature to afford a clear solution of the corresponding Na-salt. A solution of neat trans-4-isopropylcyclohexanecarboxyl chloride (IPCHAC, 9.02 g, 1.01 equiv) was added to the solution of Phe-OH obtained above, over 3 min, while stirring at room temperature. The rest of the IPCHAC in the funnel was washed with toluene (1 mL) and added. The resulting mixture was stirred for 1 h, and was treated with 10% HCl (32 mL) to adjust the pH to 3, while stirring. The mixture was stirred for 1 h, and filtered. The solid was washed with water (200 mL) and sucked well to afford 33.3 g of the moist product, which lost weight after drying at 78°/2.2 mbar (Assay 98.4%, purity >99%, yield 86%).

ST nateglinide **crystal** form prepn polymorphism dosage form

IT **Crystal morphology**
Crystallization
Drug delivery systems
Polymorphism (**crystal**)
Precipitation (chemical)
Pulverization
Solvents

(preparation of crystalline form of nateglinide for dosage forms)

IT **105816-04-4P, Nateglinide**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(preparation of crystalline form of nateglinide for dosage forms)

L11 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2005:55192 CAPLUS

DN 142:156316

TI A saponification and neutralization process for the preparation of chirally pure nateglinide from its lower alkyl esters and nateglinide polymorphic **crystalline** modifications

IN Gazdag, Maria; Gizur, Tibor; Hegedus, Bela; Szemzo, Attila; Tarkanyi, Gabor; Toerley, Jozsef; Babjak, Monika

PA Richter Gedeon Vegyeszeti Gyar Rt., Hung.

SO PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005005373	A1	20050120	WO 2004-HU73	20040708
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI HU 2003-2174 A 20030710

OS CASREACT 142:156316

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI A saponification and neutralization process for the preparation of chirally pure nateglinide from its lower alkyl esters and nateglinide polymorphic **crystalline** modifications

ST nateglinide ester sapon neutralization prepn polymorphic cryst; **crystal** polymorph nateglinide PREPN

IT Neutralization

Polymorphism (**crystal**)

(saponification and neutralization process for the preparation of chirally pure nateglinide from its lower alkyl esters and nateglinide polymorphic crystalline modifications)

IT **105816-04-4P, Nateglinide**

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)

(saponification and neutralization process for the preparation of chirally

pure

nateglinide from its lower alkyl esters and nateglinide polymorphic

crystalline modifications)

L11 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:648496 CAPLUS

DN 141:179640

TI Preparation of a polymorphic **crystalline** form of the antidiabetic agent nateglinide

IN Frenkel, Gustavo; Gome, Boaz; Wizel, Shlomit

PA Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.

SO PCT Int. Appl., 124 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004067496	A1	20040812	WO 2004-US839	20040113
	WO 2004067496	C2	20041209		
	W:	AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI			
	WO 2004009532	A1	20040129	WO 2003-US322375	20030718
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	US 2004181089	A1	20040916	US 2003-622905	20030718
	US 2005090552	A1	20050428	US 2003-693166	20031023
	US 2005014836	A1	20050120	US 2003-746697	20031224
	CA 2513753	AA	20040812	CA 2004-2513753	20040113
	EP 1511717	A1	20050309	EP 2004-701826	20040113
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
PRAI	US 2003-442109P	P	20030123		
	US 2003-449791P	P	20030224		
	US 2003-479016P	P	20030616		
	US 2003-622905	A2	20030718		
	WO 2003-US22375	A2	20030718		
	US 2003-693166	A2	20031023		
	US 2003-746697	A2	20031224		
	US 2002-396904P	P	20020718		
	US 2002-413622P	P	20020925		
	US 2002-414199P	P	20020926		
	US 2002-423750P	P	20021105		
	US 2002-432093P	P	20021210		
	US 2002-432962P	P	20021212		
	US 2003-614266	A	20030703		
	WO 2004-US839	W	20040113		
TI	Preparation of a polymorphic crystalline form of the antidiabetic agent nateglinide				
ST	nateglinide crystal polymorphism antidiabetic				

IT **Crystallization**
 Precipitation (chemical)
 (in the preparation of a polymorphic crystalline form of the antidiabetic agent nateglinide)

IT Antidiabetic agents
 Polymorphism (**crystal**)
 (preparation of a polymorphic crystalline form of the antidiabetic agent nateglinide)

IT **105816-04-4**, Nateglinide
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preparation of a polymorphic crystalline form of the antidiabetic agent nateglinide)

L11 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2004:203799 CAPLUS

DN 140:241062

TI Process for the formation of a **crystalline** polymorphic form of nateglinide

IN Reguri, Buchi Reddy; Kadaboina, Rajasekhar; Polavarapu, Srinivas

PA Reddy's Laboratories Limited, India; Reddy's Laboratories, Inc.

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004020396	A1	20040311	WO 2003-US26880	20030827
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004077725	A1	20040422	US 2003-649380	20030827

PRAI IN 2002-MA631 A 20020828

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Process for the formation of a **crystalline** polymorphic form of nateglinide

ST **crystal** polymorphism nateglinide

IT **Crystallization**

(in a process for the formation of a crystalline polymorphic form of nateglinide)

IT Polymorphism (**crystal**)

(process for the formation of a crystalline polymorphic form of nateglinide)

IT **105816-04-4P**, Nateglinide

RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(process for the formation of a crystalline polymorphic form of nateglinide)

L11 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:892741 CAPLUS

DN 139:369757

TI Process for the preparation of a **crystal** polymorphic form of

N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide)
 IN Rajamahendra, Shanmughasamy; Aswathanarayanappa, Chandrashekar;
 Puthiaparampil, Tom Thomas; Sridharan, Madhavan; Ganesh, Sambasivam
 PA Biocon India Limited, India
 SO PCT Int. Appl., 19 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003093222	A1	20031113	WO 2002-IN114	20020429
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CA 2481322	AA	20031113	CA 2002-2481322	20020429
	EP 1499586	A1	20050126	EP 2002-733208	20020429
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
	US 2005165108	A1	20050728	US 2003-508364	20020429
	JP 2005523933	T2	20050811	JP 2004-501362	20020429
PRAI	WO 2002-IN114	W	20020429		

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Process for the preparation of a **crystal** polymorphic form of
 N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide)
 ST nateglinide prepn **crystal** polymorphism;
 isopropylcyclohexylcarbonylphenylalanine prepn **crystal**
 polymorphism
 IT Drying
 Filtration
 (in a process for the preparation of a **crystal** polymorphic form of
 N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide))
 IT Bases, reactions
 RL: RGT (Reagent); RACT (Reactant or reagent)
 (in a process for the preparation of a **crystal** polymorphic form of
 N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide))
 IT Acids, reactions
 RL: RGT (Reagent); RACT (Reactant or reagent)
 (inorg.; in a process for the preparation of a **crystal** polymorphic
 form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine
 (nateglinide))
 IT Diabetes mellitus
 (non-insulin-dependent; process for the preparation of a **crystal**
 polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-
 phenylalanine (nateglinide) for the treatment of)
 IT Antidiabetic agents
 Polymorphism (**crystal**)
 (process for the preparation of a **crystal** polymorphic form of
 N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide))
 IT Ligroine
 RL: NUU (Other use, unclassified); USES (Uses)
 (solvent; process for the preparation of a **crystal** polymorphic
 form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine
 (nateglinide))

IT 1344-28-1, Alumina, uses
 RL: NUU (Other use, unclassified); USES (Uses)
 (base support; in a process for the preparation of a **crystal** polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide))

IT 110-86-1, Pyridine, reactions 121-44-8, Triethylamine, reactions 497-19-8, Sodium carbonate, reactions 584-08-7, Potassium carbonate 1310-58-3, Potassium hydroxide, reactions 1310-65-2, Lithium hydroxide 1310-73-2, Sodium hydroxide, reactions
 RL: RGT (Reagent); RACT (Reactant or reagent)
 (base; in a process for the preparation of a **crystal** polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide))

IT 7077-05-6, trans-4-Isopropylcyclohexanecarboxylic acid 13033-84-6, D-Phenylalanine methyl ester hydrochloride
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (in a process for the preparation of a **crystal** polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide))

IT 71760-04-8, Propanephosphonic acid anhydride
 RL: RGT (Reagent); RACT (Reactant or reagent)
 (mineral acid; in a process for the preparation of a **crystal** polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide))

IT 105816-04-4P, Nateglinide
 RL: IMF (Industrial manufacture); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); PREP (Preparation); PROC (Process)
 (process for the preparation of a **crystal** polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide))

IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, Isopropanol, uses 75-09-2, Dichloromethane, uses 141-78-6, Ethyl acetate, uses 1300-21-6, Dichloroethane 7732-18-5, Water, uses
 RL: NUU (Other use, unclassified); USES (Uses)
 (solvent; process for the preparation of a **crystal** polymorphic form of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine (nateglinide))

L11 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2003:837030 CAPLUS
 DN 139:341723
 TI Novel nateglinide **crystals**
 IN Koguchi, Yoshihito; Nakao, Tomoko; Sumikawa, Michito
 PA Ajinomoto Co., Inc., Japan
 SO PCT Int. Appl., 17 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003087039	A1	20031023	WO 2003-JP4686	20030414
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1496048	A1	20050112	EP 2003-746474	20030414

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 US 2005101672 A1 20050512 US 2004-965171 20041015
 PRAI JP 2002-111963 A 20020415
 WO 2003-JP4686 W 20030414

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Novel nateglinide **crystals**
 AB A type **crystal** (powder X-ray diffraction main peaks: 4.4°, 5.2°, 15.7°, 18.5° (2 theta)), M type **crystal** (powder X-ray diffraction main peaks: 6.0°, 14.2°, 15.2°, 18.8° (2 theta)), and P type **crystal** (powder X-ray diffraction main peaks: 4.8°, 5.3°, 14.3°, 15.2° (2 theta)) of nateglinide, which are all novel **crystals**, can be prepared by a method comprising dissolving nateglinide in a solvent exhibiting high solubility for nateglinide and then adding a solvent exhibiting poor solubility for nateglinide or dissolving nateglinide in a mixed solvent comprising a solvent exhibiting high solubility for nateglinide and a solvent exhibiting poor solubility for nateglinide and then cooling the resulting nateglinide solution to precipitate **crystals**, subjecting the product to filtration, and then drying at a specific temperature Nateglinide is a known antidiabetic.
 ST nateglinide **crystal** prepn antidiabetic
 IT **Crystal** structure
 (crystal structure of nateglinide **crystals**)
 IT Antidiabetic agents
Crystal structure types
 Drying
 Polymorphism (**crystal**)
 (preparation of A, M, and P type nateglinide **crystals** and drying of said **crystals**)
 IT **Crystallization**
 (preparation of A, M, and P type nateglinide **crystals** by crystallization from mixture of solvents)
 IT 105816-04-4P, Nateglinide
 RL: PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of A, M, and P type nateglinide **crystals** by crystallization from mixture of solvents)
 IT 64-17-5, Ethanol, uses 67-64-1, Acetone, uses 75-09-2, Methylene chloride, uses 110-54-3, Hexane, uses 123-91-1, Dioxane, uses 7732-18-5, Water, uses
 RL: NUU (Other use, unclassified); USES (Uses)
 (solvent for crystallization; preparation of A, M, and P type nateglinide **crystals** by crystallization from mixture of solvents)
 L11 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2003:762699 CAPLUS
 DN 140:64875
 TI Study of nateglinide polymorphism
 AU Li, Gang; Xu, Qunwei; Yao, Jie; Su, Guoqiang; Wang, Fang
 CS Chemistry and Physics Central- laboratory, Nanjing Normal University, Nanjing, 210097, Peop. Rep. China
 SO Huagong Shikan (2002), 16(7), 17-18
 CODEN: HUSHFT; ISSN: 1002-154X
 PB Huagong Shikan Zazhishe
 DT Journal
 LA Chinese
 AB The **crystal** structure of nateglinide called an S form determined by an x-ray powder diffraction method. The pattern, data, and **crystal** size were obtained. The m.p. was determined by DSC as 172.04°.

ST nateglinide polymorphism **crystal** structure
IT Polymorphism (**crystal**)
(nateglinide polymorphism)
IT **Crystal** structure
(of nateglinide polymorph)
IT **105816-04-4**, Nateglinide
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(nateglinide polymorphism)

L11 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:697592 CAPLUS

DN 140:187130

TI Study on stability of nateglinide polymorphism

AU Li, Gang; Xu, Qun Wei; Mo, Xiang Yin; Chen, Jia Ying; Su, Guo Qiang

CS Chemistry and Physics Central laboratory, Nanjing Normal University,
Nanjing, 210097, Peop. Rep. China

SO Chinese Chemical Letters (2003), 14(7), 730-733

CODEN: CCLEE7; ISSN: 1001-8417

PB Chinese Chemical Society

DT Journal

LA English

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The stability of three forms of nateglinide, especially, S-form and H-form, was determined The S-form was a new **crystal** structure of nateglinide.

Three forms of nateglinide were treated under different conditions such as in various temps., humidity, light, etc. Anal. of their **crystal** structures was performed by x-ray powder diffraction and their particle shapes were observed with scanning electron microscope. The results indicated that the stability of S-form of nateglinide is the best among the three forms and their particle shapes are quite different. The S-form is the sheet structure of layer upon layer, H-form looks like a hank of silk lines and the B-form is of clubbed shape.

IT **Crystal** structure

(of nateglinide and stability of polymorphs)

IT Polymorphism (**crystal**)

Thermal stability

(stability of nateglinide polymorphs)

IT **105816-04-4**, Nateglinide

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)

(stability of nateglinide polymorphs)

L11 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:686087 CAPLUS

DN 140:292376

TI Study on the **crystal** types of nateglinide

AU Sun, Piaoyang; Gou, Shaohua; Ma, Yonglin

CS State Key Laboratory of Coordination Chemistry, Nanjing University,
Nanjing, 210093, Peop. Rep. China

SO Huaxue Yanjiu Yu Yingyong (2002), 14(4), 457-458, C3

CODEN: HYYIFM; ISSN: 1004-1656

PB Huaxue Yanjiu Yu Yingyong Bianjibu

DT Journal

LA Chinese

TI Study on the **crystal** types of nateglinide

AB N-(trans-4-methylethylcyclohexylcarbonyl)-D-phenylalanine, nateglinide, is an effective drug to decrease blood sugar, which is under clin. trials in China. This compound has been reported to have two **crystal** types, one of which is more suitable to prepare the drug. The nateglinide with different **crystal** types was prepared Their m.ps., TGA-DTA and DSC

spectral data, LR and X-ray powder diffraction spectra of all samples were studied with different **crystal** types. A new **crystal** type that has not been reported in the literature was discovered. The method for controlling the **crystal** type was also presented.

IT Antidiabetic agents

Crystal morphology

Crystal structure

Human

Polymorphism (**crystal**)

(polymorphism of nateglinide)

IT 105816-04-4, Nateglinide

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(polymorphism; polymorphism of nateglinide)

L11 ANSWER 12 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:221492 CAPLUS

DN 138:243310

TI Novel stable **crystal** form of N-trans-4-

isopropylcyclohexylcarbonyl)-D-phenylalanine and process of preparation

IN Shah, Vrajesh; Hitkari, Anurag; Deo, Keshav; Rengaraju, Srinivasan

PA Alembic Limited, India

SO PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003022251	A1	20030320	WO 2001-IB2080	20011105
	W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, ES, GD, GE, HR, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PH, PL, RO, SG, SI, SK, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	IN 191354	A	20031129	IN 2001-MU872	20010912
	EP 1435912	A1	20040714	EP 2001-978760	20011105
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI	IN 2001-MU871	A	20010912		
	IN 2001-MU872	A	20010912		
	WO 2001-IB2080	W	20011105		

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Novel stable **crystal** form of N-trans-4-

isopropylcyclohexylcarbonyl)-D-phenylalanine and process of preparation

AB A stable **crystal** form of N-(trans-4-isopropylcyclohexylcarbonyl)-

D-phenylalanine (I) may be produced by crystallization of I with a solvent at

25 -

38 °C and forming **crystals** in the solvent. The

crystal form may be formed by recrystn. out of solution The

crystal form obtained in this way have different m.p., infra red

spectrum and X-ray diffraction patterns from previously known forms

"B-type" and "H-Type" of the compound

ST phenylalanine isopropylcyclohexylcarbonyl **crystal** form

IT **Crystal** structure

(of N-trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine)

IT **Crystal** morphology

(stable **crystal** form of N-trans-4-

isopropylcyclohexylcarbonyl)-D-phenylalanine)

IT 105816-04-4
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
 (stable **crystal** form of N-trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine)

IT 68-12-2, Dmf, processes 75-05-8, Acetonitrile, processes 127-19-5, Dimethylacetamide
 RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)
 (stable **crystal** form of N-trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine)

L11 ANSWER 13 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2003:146027 CAPLUS
 DN 139:235199
 TI Study on stability of nateglinide polymorphism
 AU Li, Gang; Xu, Qun-Wei; Mo, Xiang-Yin; Chen, Jia-Ying; Su, Guo-Qiang
 CS Testing & Analysis Center, Nanjing Normal University, Nanjing, 210097, Peop. Rep. China
 SO Huaxue Xuebao (2003), 61(2), 291-294
 CODEN: HHHPA4; ISSN: 0567-7351
 PB Kexue Chubanshe
 DT Journal
 LA Chinese
 AB A study has been made on the stability of three forms of nateglinide treated in different conditions, such as temperature, humidity, irradiation and so on. Anal. of the **crystal** structure was performed by x-ray powder diffraction. Their particle shapes were observed in scan electron microscope. The results show that the stability of S-form of nateglinide is the best among the three forms.

IT Polymorphism (**crystal**)
 X-ray diffraction
 (stability of nateglinide polymorphism)

IT 105816-04-4, Nateglinide
 RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (stability of nateglinide polymorphism)

L11 ANSWER 14 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2002:813874 CAPLUS
 DN 137:311199
 TI Amino acid complexes of C-aryl glucosides for treatment of diabetes
 IN Gougoutas, Jack Z.
 PA Bristol-Myers Squibb Company, USA
 SO PCT Int. Appl., 80 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002083066	A2	20021024	WO 2002-US11066	20020408
	WO 2002083066	A3	20030306		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2444481 AA 20021024 CA 2002-2444481 20020408
 US 2003064935 A1 20030403 US 2002-117914 20020408
 US 6774112 B2 20040810
 EP 1385856 A2 20040204 EP 2002-723801 20020408

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2004536047 T2 20041202 JP 2002-580871 20020408

PRAI US 2001-283097P P 20010411
 WO 2002-US11066 W 20020408

OS MARPAT 137:311199

ST **crystal** structure amino acid complex aryl glucoside; amino acid complex aryl glucoside prepn antidiabetic

IT Antidiabetic agents
 Antiobesity agents
 Atherosclerosis
Crystal structure
 Diabetes mellitus
 Human
 Hyperglycemia
 Hypertension
 Hypertriglyceridemia
 Hypolipemic agents
 Obesity
 (preparation of amino acid/C-aryl glucoside complexes for treatment of diabetes and related diseases)

IT 51-64-9, Dexamphetamine 94-20-2, Chlorpropamide 122-09-8, Phentermine 637-07-0, Clofibrate 657-24-9, Metformin 9004-10-8, Insulin, biological studies 10238-21-8, Glyburide 14838-15-4, Phenylpropanolamine 21187-98-4, Gliclazide 22232-71-9, Mazindol 25812-30-0, Gemfibrozil 29094-61-9, Glipizide 49562-28-9, Fenofibrate 56180-94-0, Acarbose 72432-03-2, Miglitol 75330-75-5, Lovastatin 79902-63-9, Simvastatin 81093-37-0, Pravastatin 93479-97-1, Glimepiride 93957-54-1, Fluvastatin 96829-58-2, Orlistat 97240-79-4, Topiramate 97322-87-7, Troglitazone 105816-04-4, Nateglinide 106650-56-0, Sibutramine 111025-46-8, Pioglitazone 122320-73-4, Rosiglitazone 134523-00-5, Atorvastatin 135062-02-1, Repaglinide 141750-63-2, Nisvastatin 141758-74-9, AC2993 144288-97-1, TS 962 145599-86-6, Cerivastatin 147511-69-1, Pitavastatin 152755-31-2, LY295427 159183-92-3, L750355 161600-01-7, Isaglitazone 166518-60-1, Avasimibe 170861-63-9, JTT-501 176435-10-2, LY315902 178759-95-0, MD 700 196808-45-4 199113-98-9, NN-2344 199914-96-0, YM-440 213252-19-8, KRP297 244081-42-3, AJ9677 282526-98-1, ATL-962 287714-41-4, Rosuvastatin 335149-08-1, L895645 335149-14-9, R-119702 335149-15-0, KAD1129 335149-17-2, ARHO39242 335149-19-4, GW-409544 335149-23-0, NVPDPP-728A 335149-25-2, CP331648 430433-17-3, Glipyrider 444069-80-1, Axokine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (preparation of amino acid/C-aryl glucoside complexes for treatment of diabetes and related diseases)

L11 ANSWER 15 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:811385 CAPLUS

DN 139:12440

TI Identification of nateglinide and its **crystal** forms in nateglinide tablets using IR Spectra subtraction techniques

AU Lin, Kejiang; Chen, Wei; Tang, Weiguo; You, Qidong

CS Department of Medicinal Chemistry, China Pharmaceutical University, Nanjing, 21009, Peop. Rep. China

SO Zhongguo Yaoke Daxue Xuebao (2002), 33(2), 124-126

CODEN: ZHYXE9; ISSN: 1000-5048

PB Zhongguo Yaoke Daxue

DT Journal

LA Chinese

TI Identification of nateglinide and its **crystal** forms in

nateglinide tablets using IR Spectra subtraction techniques

AB The innovational identification method of IR (eliminated method) for detection of the **crystal** form of nateglinide in preps. was presented. The IR spectrum by spectra subtraction techniques was obtained by subtracting IR spectrum after adding small volume of solvent to eliminate nateglinide from the spectrum of nateglinide tablets' KBr disk to identify the **crystal** form of nateglinide. The method (eliminated method) was useful in identification of the nateglinide **crystal** form in preps:

ST nateglinide tablet **crystal** form IR spectra

IT **Crystal** morphology

IR spectra

(identification of nateglinide and its **crystal** forms in nateglinide tablets using IR spectra subtraction techniques)

IT Drug delivery systems

(tablets; identification of nateglinide and its **crystal** forms in nateglinide tablets using IR spectra subtraction techniques)

IT 105816-04-4, Nateglinide

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(identification of nateglinide and its **crystal** forms in nateglinide tablets using IR spectra subtraction techniques)

L11 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:609152 CAPLUS

DN 138:254901

TI a new synthesis method of nateglinide as antidiabetic drug

AU Wang, Dun; Liang, Yiheng; Gong, Ping; Zhao, Yanfang

CS School of Pharmaceutical Engineering, Shenyang Pharmaceutical University, Shenyang, 110016, Peop. Rep. China

SO Zhongguo Yaowu Huaxue Zazhi (2002), 12(2), 94-96

CODEN: ZYHZEJ; ISSN: 1005-0108

PB Zhongguo Yaowu Huaxue Zazhi Bianjibu

DT Journal

LA Chinese

OS CASREACT 138:254901

AB A new antidiabetic drug-nateglinide was synthesized from isopropylbenzene by Friedel-Crafts reaction, chloroform reaction, catalytic hydrogenation to obtain trans-4-isopropylhexanecarboxylic acid, acylation of D-phenylalanine Et ester, hydrolysis to obtain nateglinide B-type **crystal**, and **crystal**-conversion. The total yield was 9.8%.

IT **Crystal** structure types

(type B; of nateglinide as antidiabetic drug)

IT 105816-04-4P, Nateglinide

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis of nateglinide as antidiabetic drug)

L11 ANSWER 17 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:391524 CAPLUS

DN 136:374894

TI Nateglinide-containing hydrophilic drug preparations

IN Ninomiya, Nobutaka; Makino, Chisato; Yabuki, Akira

PA Ajinomoto Co., Inc., Japan

SO PCT Int. Appl., 26 pp.

CODEN: PIXXD2

DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002040010	A1	20020523	WO 2001-JP9292	20011023
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001096000	A5	20020527	AU 2001-96000	20011023
	CA 2426764	AA	20030423	CA 2001-2426764	20011023
	BR 2001014897	A	20030812	BR 2001-14897	20011023
	EP 1334721	A1	20030813	EP 2001-976818	20011023
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2004029968	A1	20040212	US 2003-420886	20030423
PRAI	JP 2000-324374	A	20001024		
	WO 2001-JP9292	W	20011023		

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Hydrophilic drug prepns. contain nateglinide B **crystals** useful as a hypoglycemic agent as the active ingredient which comprises a hydrophilic substance selected from the group consisting of hydrophilic polymers, surfactants, sugars, sugar alcs. and salts, and thus have a contact angle of the preparation surface to water of 111° or less. These prepns., which are rapid release prepns. having high elution properties, can be easily produced.

IT **Crystals**

(hypoglycemic hydrophilic drug prepns. containing nateglinide)

IT **105816-04-4, Nateglinide**

RL: BCP (Biochemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(hypoglycemic hydrophilic drug prepns. containing)

L11 ANSWER 18 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:314896 CAPLUS

DN 136:325825

TI Process for producing nateglinide **crystals**

IN Takahashi, Daisuke; Nishi, Seiichi; Takahashi, Satoji

PA Ajinomoto Co., Inc., Japan

SO PCT Int. Appl., 14 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002032854	A1	20020425	WO 2001-JP9069	20011016
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,				

BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001094265	A5	20020429	AU 2001-94265	20011016
CA 2425538	AA	20030410	CA 2001-2425538	20011016
EP 1334963	A1	20030813	EP 2001-974875	20011016

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

BR 2001014729	A	20031014	BR 2001-14729	20011016
US 2004030182	A1	20040212	US 2003-418105	20030418

PRAI JP 2000-317604 A 20001018
 WO 2001-JP9069 W 20011016

OS CASREACT 136:325825

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Process for producing nateglinide **crystals**

AB A process for producing nateglinide **crystals** comprises reacting trans-4-isopropylcyclohexylcarbonyl chloride with D-phenylalanine in a mixed solvent consisting of a ketone solvent and water in the presence of an alkali to obtain a reaction mixture containing nateglinide, adding an acid to

the reaction mixture to make it acidic, and regulating (a) the temperature to 58° to 72° and (b) and the ketone solvent concentration to > 8 weight% and < 22 weight%, to conduct crystallization Nateglinide is a known

antidiabetic.

The process is an industrially advantageous method for crystallizing nateglinide.

ST nateglinide **crystal** prepn antidiabetic

IT **Crystal** structure

(**crystal** structure of nateglinide)

IT **Crystallization**

(process for producing nateglinide **crystals**)

IT Alkali metal hydroxides

RL: RGT (Reagent); RACT (Reactant or reagent)

(process for producing nateglinide **crystals**)

IT Ketones, uses

RL: NUU (Other use, unclassified); USES (Uses)

(solvents; process for producing nateglinide **crystals**)

IT 105816-04-4P, Nateglinide

RL: IMF (Industrial manufacture); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(process for producing nateglinide **crystals**)

IT 673-06-3, D-Phenylalanine 84855-54-9

RL: RCT (Reactant); RACT (Reactant or reagent)

(process for producing nateglinide **crystals**)

IT 1310-58-3, Potassium hydroxide, reactions 7647-01-0, Hydrochloric acid, reactions

RL: RGT (Reagent); RACT (Reactant or reagent)

(process for producing nateglinide **crystals**)

IT 67-64-1, Acetone, uses 7732-18-5, Water, uses

RL: NUU (Other use, unclassified); USES (Uses)

(solvent; process for producing nateglinide **crystals**)

L11 ANSWER 19 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:234892 CAPLUS

DN 137:39555

TI Detection of **crystal** polymorphs of nateglinide by DSC

AU Lin, Kejiang; Chen, Wei; You, Qidong

CS China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China

SO Yaoxue Xuebao (2002), 37(1), 46-49

CODEN: YHHPAL; ISSN: 0513-4870

PB Yaoxue Xuebao Bianjibu

DT Journal

LA Chinese

TI Detection of **crystal** polymorphs of nateglinide by DSC

AB The differential scanning calorimetric (DSC) methodol. for controlling the **crystal**-type B form of nateglinide was presented. Pure fine powder of **crystal**-type B and H of nateglinide dried with P2O5 as desiccant at 80° in vacuum for 4 h was measured dQ/dT by DSC at heating rate of 10° min⁻¹ and temperature between 100° and 200° to calculate the enthalpy ΔHB and ΔHH. Uniform mixts. of **crystal**-type B and H of dried fine powder of nateglinide in different proportions were accurately weighed. The enthalpy of the mixts. was measured by DSC as above to calculate the enthalpy (ΔH). Using B% as X, ΔH as parameters, the regression equation was obtained. Based on this equation, the unknown composition of mixed **crystal** was evaluated by yδH values. The method was used to control the limitation of **crystal**-type B of nateglinide by the HδH value of mixture of known composition as reference. The results measured from different labs. showed that the repeatability was 0.61% and recoveries were 86.2-127% when the amount of **crystal**-type B was between 0-15%. This method can be used to evaluate the **crystal**-type B composition of nateglinide.

ST nateglinide **crystal** polymorph control

IT **Crystal** growth
Differential scanning calorimetry
(control of polymorphism during **crystal** growth of nateglinide detected by DSC)

IT Polymorphism (**crystal**)
(detection of **crystal** polymorphs of nateglinide by DSC)

IT Enthalpy
(of polymorphism of nateglinide **crystals**)

IT 105816-04-4, Nateglinide
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); PROC (Process)
(detection of **crystal** polymorphs of nateglinide by DSC)

L11 ANSWER 20 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:130037 CAPLUS

DN 137:325603

TI Synthesis of Nateglinide

AU Zhu, Xue-yan; Peng, Ka; Wang, Xiao-qin; Yang, Li-ping

CS Dep. Chem., East China Normal Univ., Shanghai, 200062, Peop. Rep. China

SO Hecheng Huaxue (2001), 9(6), 537-540
CODEN: HEHUE2; ISSN: 1005-1511

PB Hecheng Huaxue Bianjibu

DT Journal

LA Chinese

OS CASREACT 137:325603

IT 105816-04-4DP, Nateglinide, B **crystal** type
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and crystalline forms of)

IT 105816-04-4DP, H **crystal** type
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of Nateglinide)

L11 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:844448 CAPLUS

DN 136:159110

TI A new **crystal** structure in nateglinide found by X-ray powder diffraction

AU Li, Gang; Su, Guo-qiang; Xu, Qun-wei

CS Center for Analysis & Measurement, Nanjing Normal University, Nanjing, 210097, Peop. Rep. China

SO Yaowu Fenxi Zazhi (2001), 21(5), 342-344
 CODEN: YFZADL; ISSN: 0254-1793
 PB Yaowu Fenxi Zazhi Bianji Weiyuanhui
 DT Journal
 LA Chinese
 TI A new **crystal** structure in nateglinide found by X-ray powder diffraction
 AB A new **crystal** structure being assigned as S-form was found in nateglinide. The x-ray pattern and data were given and the m.p. was determined. Phase anal. was carried out by x-ray powder diffraction; the m.ps. were determined by DSC. S-form nateglinide was different from the H or B **crystal** form. The m.p. was 172.04°. S-form nateglinide was a new **crystal** form. X-ray powder diffraction anal. was one of the most effective methods for phase structure characterization.
 ST **crystal** structure nateglinide
 IT **Crystal** structure
 Molecular structure
 (of nateglinide)
 IT 105816-04-4, Nateglinide
 RL: PRP (Properties)
 (**crystal** structure of)

L11 ANSWER 22 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2001:625224 CAPLUS
 DN 136:348527
 TI New **crystal** form of nateglinide
 AU Li, Gang; Su, Guoqiang; Xu, Qunwei; Zhu, Chongquan
 CS Chemistry and Physics Central Laboratory, Nanjing Normal University, Nanjing, 210097, Peop. Rep. China
 SO Yaoxue Xuebao (2001), 36(7), 532-534
 CODEN: YHHPAL; ISSN: 0513-4870
 PB Yaoxue Xuebao Bianjibu
 DT Journal
 LA Chinese
 TI New **crystal** form of nateglinide
 AB The S form **crystals** of nateglinide [N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine] were studied by XRD, IR, elemental anal., and differential scan calorimetry. The S-form nateglinide **crystal** was different from the H-form or B-form. The m.p. was 172.04°. The results showed that the S-form nateglinide was a new **crystal** form.
 ST nateglinide X ray **crystallog** study
 IT **Crystal** structure
 (**crystal** structure of nateglinide **crystals**
 (S-form))
 IT 105816-04-4, Nateglinide
 RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (new **crystal** form of nateglinide)

L11 ANSWER 23 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN
 AN 2001:283772 CAPLUS
 DN 134:285620
 TI Method of treating metabolic disorders with nateglinide
 IN Gatlin, Marjorie Regan; Pongowski, Michele; Dunning, Beth
 PA Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
 SO PCT Int. Appl., 28 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001026639	A2	20010419	WO 2000-EP9816	20001006
	WO 2001026639	A3	20020110		
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1218015	A2	20020703	EP 2000-972695	20001006
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
PRAI	US 1999-415307	A	19991008		
	US 1999-415308	A	19991008		
	WO 2000-EP9816	W	20001006		

IT **Crystal** morphology

(of nateglinide; treating metabolic disorders with nateglinide)

IT 103-82-2D, Phenylacetic acid, derivs. 657-24-9, Metformin 2295-31-0D, Thiazolidinedione, derivs. 9004-10-8, Insulin, biological studies 56180-94-0, Acarbose 105816-04-4, Nateglinide 135062-02-1, Repaglinide

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (treating metabolic disorders with nateglinide)

L11 ANSWER 24 OF 25 CAPLUS COPYRIGHT 2005 ACS on STN

AN 1995:964992 CAPLUS

DN 124:155974

TI **Crystals** of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine and methods for preparing them

IN Sumikawa, Michito; Koguchi, Yoshihito; Ohgane, Takao; Irie, Yasuo; Takahashi, Satoji

PA Ajinomoto Co., Inc., Japan

SO U.S., 12 pp. Cont.-in-part of U.S. Ser. No. 166,144.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5463116	A	19951031	US 1994-190460	19940202
	US 5488150	A	19960130	US 1993-166144	19931214
	CA 2114678	AA	19950802	CA 1994-2114678	19940201
	CA 2114678	C	19990427		
PRAI	JP 1991-189696	A	19910730		
	JP 1991-199453	A	19910808		
	US 1992-921224	B1	19920729		
	US 1993-166144	A2	19931214		

TI **Crystals** of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine and methods for preparing them

AB Stable **crystals** of N-(trans-4-isopropylcyclohexylcarbonyl)-D-phenylalanine for pharmaceutical formulation may be produced by treating this compound with a solvent at a temperature of at least 10° and forming **crystals** in the solvent at a temperature of at least 10°. For example, **crystals** may be formed by crystallization out of solution, or may be formed from solid particles of the compound suspended in a solvent. **Crystals** formed in this way have different m.p., IR spectrum and

X-ray diffraction patterns from previously known forms of the compound and have enhanced processability, e.g., stability to grinding.

IT **Crystallization**

Solvent effect

(crystallization of (isopropylcyclohexylcarbonyl)phenylalanine for enhanced stability to grinding)

IT **105816-04-4**

RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(crystallization of (isopropylcyclohexylcarbonyl)phenylalanine for enhanced stability to grinding)

IT **173653-89-9**

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(crystallization of (isopropylcyclohexylcarbonyl)phenylalanine for enhanced stability to grinding)

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